US-PAT-NO: 5593673

DOCUMENT-IDENTIFIER: US 5593673 A

TITLE: Isolated porcine pancreatic cells for use in treatment of diseases characterized by insufficient insulin activity

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Brief Summary Text - BSTX (7):

The present invention provides porcine pancreatic cell(s) which can be used to generate populations of cells useful for transplantation into diabetic subjects. The porcine pancreatic cells of the invention are capable of proliferating in vitro and in vivo and are insulin-secreting after transplantation into a recipient subject. Accordingly, the invention pertains to isolated non-insulin-secreting porcine pancreatic cells having the ability to differentiate into insulin-secreting cells upon introduction into a xenogeneic subject. In one embodiment, the non-insulin-secreting porcine pancreatic cells are embryonic pancreatic cells isolated during certain stages of gestational development. It has been discovered that such porcine embryonic pancreatic cells can be maintained in culture if sub-confluent and will proliferate for long periods of time, e.g., six months or more, without forming pseudo islet-like aggregates. Preferably, the pancreatic cells are obtained from embryonic pigs at an early stage of development (i.e., prior to formation of islets in vivo) and are maintained in culture to allow cell proliferation

US-PAT-NO: 5646035

DOCUMENT-IDENTIFIER: US 5646035 A

TITLE: Method for preparing an expanded culture and clonal strains of pancreatic, thyroid or parathyroid cells

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Detailed Description Text - DETX (23):
In a similar experiment, clonal strains of human pancreatic islet cells showed specialization. Two clones of 27 tested, named HPSL-SU and HPSL-SD, apparently represented delta cells because when these cloned cultures were incubated for 24 hours in medium with no insulin and high (20 mM) glucose, they respectively produced 570 and 116 pg/ml of somatostatin (a distinctive hormonal product of delta cells). In high insulin (15 .mu.g/ml) and low glucose (2.5 mM) medium, these cloned cultures respectively produced only 9.6 and 28 pg/ml of somatostatin, thereby showing the anticipated lower response to these physiological conditions. Six of 27 clones produced low but significant amounts of insulin, ranging 88.5 to 114 pg/ml/24 hrs. None of the 27 clones made sufficient glucagon to be detected under these culture conditions.

Detailed Description Text - DETX (32):
The population doubling time was about 2.7 days over the 73 days of the study. The amount of insulin produced in response to glucose challenge was found to be about 19 ng per mg cell protein per hour at PDL #8-10. It was also

noted that the HPSL-8 monolayer cultures contain glucagon and somatostatin producing cells in addition to the insulin and C-peptide producing cells.

Detailed Description Text - DETX (36):

Time course assays using a standard RIA-type assay as in Examples 5, 6, and 7 were performed on culture medium of HPSL-8 cultures for insulin, C-peptide, glucagon, and somatostatin, and the results thereof are shown in FIGS. 3-5. At each time point in these graphs, four modifications of the basic Coon's 4506.07 medium formulation were used, whereby the tested cell culture was incubated in the modified medium for one week prior to the glucose challenge described above. Modification A was low calcium (0.35 mM CaCl.sub.2.2H.sub.2 O); modification B was low calcium plus 10 .mu.g/ml added human placental lactogen; modification C was high calcium (2.2 mM); and modification D was high calcium plus 10 .mu.g/ml added human placental lactogen. The accumulation over time of insulin, C-peptide, glucagon, and somatostatin are illustrated in Graphs A, B, C, and D, respectively, of FIGS. 3-5. The y-axis is in units of hormone accumulated, namely pg hormone accumulated/mg cell protein/ml.+-.s.e.m.; the x-axis is in units of time, namely minutes.

US-PAT-NO: 6001647

DOCUMENT-IDENTIFIER: US 6001647 A
See image for Certificate of Correction

TITLE: In vitro growth of functional islets of Langerhans and
in vivo uses thereof

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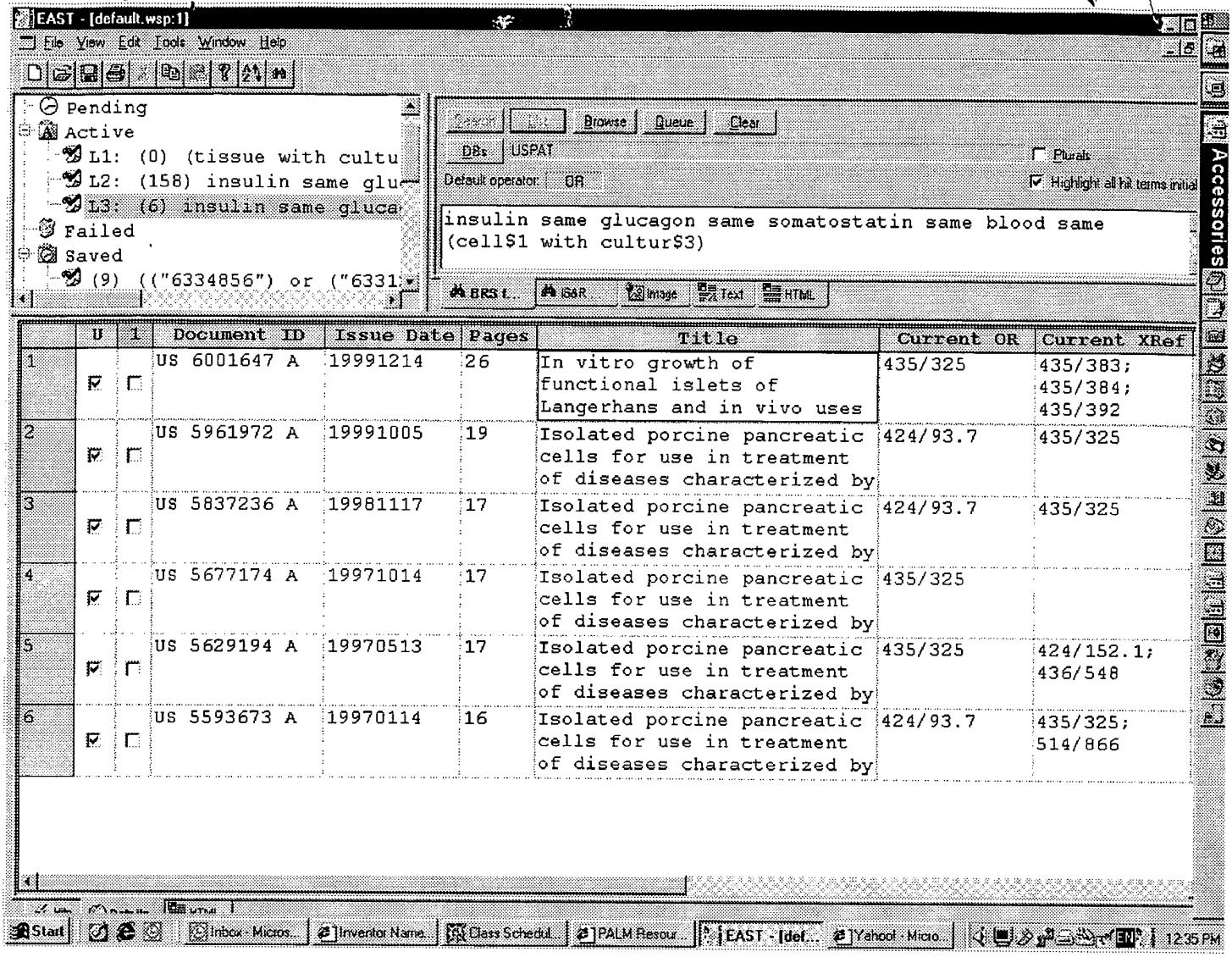
Brief Summary Text - BSTX (23):
The novel methods of the subject invention take advantage of the discovery that IPSCs exist even in the pancreas of adult individuals. The cells can be cultured in a minimal, high amino acid nutrient medium that is supplemented with normal serum which is preferably derived from the same mammalian species which serves as the origin of the islet cells (homologous serum). Several discrete phases of cell growth result in selection of IPSCs and subsequent progeny which are then induced to differentiate and form islet-like structures which are distinguishable from pseudo-islet or pseudo-pancreatic tissue of the prior art. In a first phase, primary culture of cells from a pancreas are placed in a low serum, low glucose, high amino-acid basal medium. This culture is then left undisturbed for s veral weeks to permit establishment of stromal cells and to allow the vast majority of differentiated cells to die. Once this stromal cell layer is mature, cell differentiation can be initiated by re-feeding the cell culture with the high amino acid medium supplemented with homologous normal serum plus glucose. After an additional period of growth, functional islets containing cells which produce insulin,



	U	1	Document ID	Issue Date	Pages	Title	Current OR	Current XRef
1	☑	☐	US 6001647 A	19991214	26	In vitro growth of functional islets of Langerhans and in vivo uses	435/325	435/383; 435/384; 435/392
2	☑	☐	US 5961972 A	19991005	19	Isolated porcine pancreatic cells for use in treatment of diseases characterized by	424/93.7	435/325
3	☑	☐	US 5837236 A	19981117	17	Isolated porcine pancreatic cells for use in treatment of diseases characterized by	424/93.7	435/325
4	☑	☐	US 5677174 A	19971014	17	Isolated porcine pancreatic cells for use in treatment of diseases characterized by	435/325	
5	☑	☐	US 5629194 A	19970513	17	Isolated porcine pancreatic cells for use in treatment of diseases characterized by	435/325	424/152.1; 436/548
6	☑	☐	US 5593673 A	19970114	16	Isolated porcine pancreatic cells for use in treatment of diseases characterized by	424/93.7	435/325; 514/866